for example, at page 17, lines 28-30, which indicate that a substantially pure PAMP polypeptide can have the amino acid sequence SEQ ID NO: 2, and at page 20, lines 16-22, which indicates that SEQ ID NO: 2 can be modified, for example, by substitution of one or more conservative amino acid residues.

New claim 27 is directed to a substantially pure PAMP polypeptide that contains the amino acid sequence shown as SEQ ID NO: 2. New claim 27 is supported, for example, by original claim 10 and in the specification, for example, at page 17, lines 28-30, which indicate that a substantially pure PAMP polypeptide of the invention can have the amino acid sequence SEQ ID NO: 2.

New claim 28 is directed to a substantially pure PAMP polypeptide that contains an amino acid sequence having at least 90% amino acid identity with at least 350 residues of SEQ ID NO: 2, where the 350 residues include residues 1075 to 1382 of SEQ ID NO: 2. New claim 28 is supported throughout the specification, for example, at page 19, lines 19-24, which indicate that the term "PAMP polypeptide" means a polypeptide having at least 350 of the 1382 residues of human PAMP, and at page 19, lines 24-27, which disclose the PAMP fragment having residues 1075 to 1382. Claim 28 further is supported in the specification, for example, at page 19, lines 9-15, which indicate that a PAMP polypeptide can have 90% or more sequence identity to human PAMP (SEQ ID NO: 2).

New claim 29 is directed to a substantially pure PAMP polypeptide that contains an amino acid sequence having at least 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, where the 350 residues include residues 1075 to 1382 of SEQ ID NO: 2. New claim 29 is supported throughout the specification, as described above in regard to claim 28, and further is supported in the specification, for example, at page 19, lines 9-15, which indicate that a PAMP polypeptide can have 95% or more sequence identity to human PAMP (SEQ ID NO: 2).

As set forth above, each of new claims 26 to 29 is supported by the specification as originally filed. Accordingly, the Examiner is respectfully requested to enter the new claims.

II. REMARKS

Objection to the drawings

The Examiner objects to Figure 5, which contains unlabeled panels. The Examiner notes that panels A through D are referenced in the Brief Description of the Drawings. Applicant submits herewith a new version of Figure 5 in which each panel is labeled and, accordingly, respectfully requests that the Examiner withdraw the objection to Figure 5.

Rejections under 35 U.S.C. § 112, second paragraph

The rejection of claims 9 to 12 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to the term "substantially" is respectfully traversed.

Applicant submits that claims 9 to 12 are clear and definite as written and that the term "substantially pure" means a polypeptide that is substantially free from cellular components or other contaminants present with the polypeptide in nature. See the specification, for example, at page 11, lines 9-13. Thus, a "substantially pure" polypeptide is distinct from a polypeptide as it occurs in a cell in nature. In view of the above, Applicant submits that the term "substantially pure" is clear and definite and respectfully requests that the rejection under the second paragraph of 35 U.S.C. § 112 be removed.

Rejection under 35 U.S.C. § 101

The rejection of claims 9 to 12 under 35 U.S.C. § 101 as allegedly lacking utility is respectfully traversed. In view of the cancellation of claims 9 to 12, this rejection is addressed as it pertains to claims pending claims 26 to 29.

The Office Action acknowledges that the specification teaches making antibodies specific for SEQ ID NO: 2 and the detection and treating of prostate cancer. The Office Action further asserts that the utility for the polypeptide SEQ ID NO: 2 is questionable because one cannot predict that SEQ ID NO: 2 and

its variants actually exist in nature, or are expressed in a prostate-specific manner. The Office Action further asserts that, even if the claimed PAMP polypeptide is expressed in a prostate-specific manner, that this prostate specificity does not constitute a specific utility because this utility is shared by several other prostate specific polypeptides.

In regard to whether the PAMP polypeptide is expressed in nature, the specification teaches, for example, a human polypeptide having the sequence SEQ ID NO: 2, as predicted based on the nucleic acid molecule SEQ ID NO: 1 (see Figure 1 and page 19, lines 8-18). Evidence corroborating that this polypeptide is expressed in nature in prostate cells is provided herein as a Rule 132 Declaration signed by Biaoyang Lin. As further disclosed in the specification, the PAMP cDNA is expressed in a highly prostate-specific manner. As shown in Figure 4, only significant prostate expression of the transcript was detected amongst 50 different human tissues surveyed (Figure 4 and page 9, lines 10-13). Together, these results show that the protein product of a prostate-specific transcript, PAMP, is expressed in nature.

Although evidence of prostate-specific protein expression is not provided, one skilled in the art would conclude that the PAMP polypeptide is expressed specifically in prostate. In particular, the Office Action notes that protein expression does not necessarily mirror RNA expression, pointing out that predictability of protein translation and the extent of translation are not solely contingent on mRNA expression due to a

host of other factors. While it is true that the hypothetical presence of mRNA transcripts in a variety of tissues does not necessarily imply that the protein product of this transcript is expressed in the same tissues, in the present case, where significant mRNA expression is absent in tissues other than in prostate, the skilled person must conclude that significant protein expression also is absent. Combined with evidence of expression in prostate cells shown herein in the Declaration under 37 C.F.R. § 1.132, Applicant submits that one skilled in the art would conclude that the PAMP polypeptide is expressed in a prostate-specific manner.

As acknowledged by the Examiner, the utility requirement under 35 U.S.C. § 101 can be satisfied by a specific asserted utility or a well established utility. In the present case, both the use of polypeptides as immunogens for preparation of antibodies and the further use of such antibodies to differentiate tissue types are well established utilities. In this regard, guidance in the specification regarding the preparation of antibodies using a PAMP polypeptide or fragment thereof as an immunogen is provided, for example, at page 21, line 4, to page 23, line 17. Using such antibodies, if desired, in combination with other marker antibodies, one skilled in the art can type a cell line or tissue of interest. Applicant emphasizes that such methods can be practiced even in the absence of knowledge of the function of PAMP or knowledge regarding the role of PAMP in disease etiology. Thus, the claimed PAMP polypeptides have a well established utility.

In addition, anti-PAMP antibodies raised using the claimed polypeptides have the further well-established utility of being useful as part of a therapeutic antibody conjugate. Such therapeutic antibody conjugates include chemoimmunoconjugates and radioimmunoconjugates such as those incorporating radioiodine and are well established anti-cancer therapeutics as evidenced, for example, by Exhibit A attached hereto (Weiner and Adams, Oncogene 6144-6151 (2000)). Furthermore, given that the prostate is a non-essential organ, one skilled in the art understands that anti-prostate cancer therapy does not require differential recognition of normal versus cancerous prostate tissue. In view of the above, it is clear that the claimed PAMP polypeptides, which have been shown to be expressed in prostatic cells, have utility as immunogens for raising antibodies useful in anti-cancer therapeutics.

Because the claimed PAMP polypeptides have well established utilities as set forth above, the utility requirement under 35 U.S.C. § 101 is satisfied.

Regarding the need for a specific utility

The Office Action implies that a specific utility cannot be shared by other inventions, for example, shared with other prostate-specific polypeptides. Applicant asserts that there is no requirement for an absolutely unique specific utility; as an example, a variety of therapeutic agents for treating the same cancer are patented each year, irregardless of the fact that they have a common utility. Applicant would

further point out, in regard to the well established utility discussed above, that each new prostate-specific marker has utility in characterizing cell lines and tissues and that panels of markers can be used, if desired, to characterize cell line and tissue samples. Should the Examiner persist on this point, he is respectfully requested to cite his source for asserting that a specific utility cannot be "shared by several other prostate specific polypeptides" (Office Action at page 6, lines 4-6).

In sum, the claimed PAMP polypeptides have a well established utility. Accordingly, Applicant respectfully requests that the Examiner remove the rejection under 35 U.S.C. § 101.

Rejections under 35 U.S.C. § 112, first paragraph

Regarding written description

The rejection of claims 9, 11 and 12 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. The Office Action asserts that the claims read on variants of SEQ ID NO: 2, including any type of substitution besides conservative substitutions, of any amino acid, throughout the length of the polypeptide, as well as insertions and deletions. The Office Action further asserts that no common structural or functional attributes that identify the claimed variants are disclosed. In view of the cancellation of

claims 9 to 12, Applicants address this rejection as it pertains to pending claims 26, 28 and 29.

Regarding claim 26

Applicant submits that sufficient written description is provided to convey to one skilled in the art that the inventor had possession of the invention of claim 26. In particular, written description is provided for the substantially pure PAMP polypeptide of claim 26, which contains the amino acid sequence shown as SEQ ID NO: 2 or an amino acid sequence having one or more conservative substitutions relative to SEQ ID NO: 2. The specification discloses, for example, that a PAMP polypeptide can have the amino acid sequence SEQ ID NO: 2 (page 17, lines 30), and also discloses SEQ ID NO: 2 in Figure 1. The specification further provides written description by teaching that a PAMP polypeptide can have a non-naturally occurring amino acid sequence with non-naturally occurring amino acid substitutions as compared to SEQ ID NO: 2, and further teaches that modifications to SEQ ID NO: 2 include the substitution of one or more conservative amino acid residues (page 19, line 28, to page 20, line 5; page 20, lines 16-19).

Conservative substitutions are well known in the art to be substitutions in which a first amino acid is replaced by another amino acid or amino acid analog having at least one biochemical property similar to that of the first amino acid; similar properties include, for example, similar size, charge, hydrophobicity or hydrogen-bonding capacity. Thus, a

conservative substitution can be, for example, a substitution in which a first uncharged polar amino acid is conservatively substituted with a second uncharged polar amino acid such as cysteine, serine, threonine, tyrosine, glycine, glutamine or asparagine or an analog thereof; a substitution in which a first basic amino acid is conservatively substituted with a second basic amino acid such as arginine, lysine, histidine, 5-hydroxylysine, N-methyllysine or an analog thereof; a substitution in which a first hydrophobic amino acid is conservatively substituted with a second hydrophobic amino acid such as alanine, valine, leucine, isoleucine, proline, methionine, phenylalanine or tryptophan or an analog thereof; or a substitution in which a first acidic amino acid is conservatively substituted with a second acidic amino acid such as aspartic acid or glutamic acid or an analog thereof. In view of what is described in the specification and well known in the art regarding conservative substitutions, it is clear that Applicant was in possession of the substantially pure PAMP polypeptide of claim 26 at the time the application was filed.

Regarding claims 28 and 29

The specification further provides written description sufficient to convey to one skilled in the art that Applicant had possession of the invention of claims 28 and 29, directed to substantially pure PAMP polypeptides having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, including residues 1075 to 1382 of SEQ ID NO: 2. The specification provides guidance, for example, by providing at

least 350 residues of SEQ ID NO: 2, as shown in Figure 1, and by teaching structural attributes common to the PAMP polypeptides of claims 28 or 29. In this regard, the specification teaches, for example, a PAMP polypeptide having at least 90% or 95% sequence identity with SEQ ID NO: 2 (see page 19, lines 12-15). Thus, the PAMP polypeptides of claim 28 are united by the common structural attribute of sharing at least 9 out of 10 residues in common with the specified portion of SEQ ID NO: 2. Similarly, the PAMP polypeptides of claim 29 are united by the common structural attribute of sharing at least 19 out of 20 residues in common with the specified portion of SEQ ID NO: 2. Given the written description of SEQ ID NO: 2 in Figure 1 and the further structural attributes disclosed in the specification, it would have been clear to the skilled person that Applicant was in possession of the claimed invention at the time the application was filed.

In view of the above remarks, Applicant respectfully requests that the Examiner reconsider and remove the written description rejection under the first paragraph of 35 U.S.C. § 112.

Regarding enablement

The rejection of claims 9, 11 and 12 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. The Office Action asserts that the claimed invention is not supported by a well established utility and that, therefore, one skilled in the art would not have known

how to make and use the invention. In view of the cancellation of claims 9 to 12, Applicant addresses this rejection as it pertains to pending claims 26, 28 and 29.

Applicant submits that undue experimentation would not have been required to make and use the invention of claims 26, 28 and 29. As argued above, the claimed invention has a well established utility, that of preparing anti-PAMP antibodies for identification of prostate tissue. In regard to enablement and as described further below, the specification provides guidance regarding making and using PAMP polypeptides as immunogens and, given the further guidance in the specification regarding the prostate-specific expression of PAMP, one skilled in the art would have been able to use such antibodies, for example, to identify the tissue type of a sample using routine methods.

Firstly, guidance regarding making polypeptides related to SEQ ID NO: 2 is provided in Figure 1, which discloses the sequence SEQ ID NO: 2 and the encoding nucleic acid sequence SEQ ID NO: 1, and in the specification, which teaches that PAMP polypeptides can be prepared from natural sources or produced recombinantly (see Figure 1, and page 22, lines 25-30). Secondly, guidance regarding using a PAMP polypeptide as an immunogen for preparation of monoclonal and polyclonal antibodies is provided in the specification at pages 21 to 23 (see, in particular, page 21, line 31, to page 22, line 4; page 22, lines 16-24; and page 22, line 25, to page 23, line 17). Thirdly, the specification teaches that significant PAMP RNA expression was observed only in the prostate (page 9, lines 10-13). In view of

the guidance in the specification regarding preparation of PAMP polypeptides and anti-PAMP antibodies and the prostate-specific expression of PAMP transcripts, one skilled in the art would have been able to make and use the PAMP polypeptides using routine methods. Because only routine work and not undue experimentation would have been required, the specification satisfies the enablement requirement under 35 U.S.C. § 112, first paragraph. In view of the above, Applicant respectfully requests that the enablement rejection be removed.

Rejections under 35 U.S.C. § 102

withdrawn

Regarding the §102(a) rejection over Nagase et al.

The rejection of claims 9, 11 and 12 under 35 U.S.C. §102 as allegedly anticipated by Nagase et al. is respectfully traversed. The Office Action alleges that Nagase et al. (Q9HCD4) describe a sequence which is 99.8% similar to SEQ ID NO: 2, from amino acid 375 to 1279. In view of the cancellation of claims 9, 11 and 12, this rejection will be addressed as it pertains to pending claims 26, 28 and 29.

Regarding claim 26

Nagase et al. do not teach the substantially pure PAMP polypeptide of claim 26, which contains the amino acid sequence SEQ ID NO: 2 or an amino acid sequence having one or more conservative substitutions relative to SEQ ID NO: 2. At best,

Nagase et al. appear describe a sequence with similarity to a subpart of SEQ ID NO: 2, namely residues 375 to 1279. Absent the teaching of SEQ ID NO: 2 or a sequence having conservative substitutions relative to SEQ ID NO: 2, Nagase et al. cannot anticipate the invention.

Regarding claims 28 and 29

Applicant submits that the Nagase et al. sequence is not prior art with respect to claims 28 and 29, which are directed to a substantially pure PAMP polypeptide which contains an amino acid sequence having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, including residues 1075 to 1382 of SEQ ID NO: 2. A representative of the DNA Data Base of Japan has indicated that the Nagase et al. sequence identified by accession number AB046858, which is equivalent to the sequence referenced by the Examiner as Q9HCD4, was first available to the public on September 8, 2000. See Exhibits 1 and 2 of Declaration under 37 C.F.R. § 1.131.

In particular, the Nagase et al. sequence is not prior art with respect to the claimed invention because Applicant obtained the claimed sequence prior to the September 8, 2000, date accorded the accession. As evidence that the release date of the Nagase et al. sequence was not before Applicant's date of invention, Applicant submits herewith a Declaration under 37 C.F.R. § 1.131 along with copies of relevant laboratory records. The dates of the laboratory records have been redacted; however, the dates shown in the original sheets indicate that Applicant

had obtained the claimed sequence prior to September 8, 2000. Because the Nagase et al. sequence was not described more than one year prior to the filing of the above-identified application and because Applicant reduced the invention to practice before the Nagase et al. sequence was released to the public, this reference is not prior art with respect to claims 28 or 29.

Accordingly, Applicant respectfully respects that the rejection over Nagase et al. under 35 U.S.C. §102 be removed.

Regarding the §102(a) rejection over Kawakami et al.

The rejection of claims 9, 11 and 12 under 35 U.S.C. §102 as allegedly anticipated by Kawakami et al. is respectfully traversed. Kawakami et al. (Q9H5S0) allegedly describe a sequence which is 99.3% similar to SEQ ID NO: 2, from amino acid 41 to amino acid 492. In view of the cancellation of claims 9, 11 and 12, this rejection will be addressed as it pertains to pending claims 26, 28 and 29.

Regarding claim 26

As set forth above, the substantially pure PAMP polypeptide of claim 26 contains the amino acid sequence SEQ ID NO: 2 or an amino acid sequence having one or more conservative substitutions relative to SEQ ID NO: 2. The cited reference by Kawakami et al. does not anticipate the invention, since, at best, this reference describes a subpart of SEQ ID NO: 2 having residues 41 to 492. Absent the teaching of the sequence SEQ ID

NO: 2 or an amino acid sequence having conservative substitutions relative to SEQ ID NO: 2, the cited reference by Kawakami et al. cannot anticipate the invention.

Regarding claims 28 and 29

As set forth above, claims 28 and 29 are directed to a substantially pure PAMP polypeptide containing an amino acid sequence having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, including residues 1075 to 1382 of SEQ ID NO: 2. Thus, the substantially pure PAMP polypeptide of claims 28 and 29 contains a specified degree of amino acid identity to the carboxy-terminal portion of SEQ ID NO: 2. In contrast to the claimed PAMP polypeptides, Kawakami et al. describe a sequence related to the amino-terminal portion (residues 41 to 492) of SEQ ID NO: 2. Absent the teaching of an amino acid sequence having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, including residues 1075 to 1382 of SEQ ID NO: 2, the cited reference by Kawakami et al. cannot anticipate the invention.

In view of the above remarks, Applicant respectfully respects that the rejection over Kawakami et al. under 35 U.S.C. §102 be removed.

Regarding the §102(b) rejection over Steward et al.

The rejection of claims 9 and 11 under 35 U.S.C. §102 as allegedly anticipated by Steward is respectfully traversed.

In view of the cancellation of claims 9 and 11, this rejection will be addressed as it pertains to pending claims 26, 28 and 29.

Regarding claim 26

The cited reference by Steward (O46018) does not appear to teach a substantially pure PAMP polypeptide that contains the amino acid sequence SEQ ID NO: 2 or an amino acid sequence having one or more conservative substitutions relative to SEQ ID NO: 2, as set forth in claim 26. Rather, as indicated in the present Office Action, Steward describes a sequence which is 45% similar to SEQ ID NO: 2, from amino acid 724 to 1228. Thus, at best Steward reports a sequence having a low degree of similarity to a subpart of SEQ ID NO: 2 but does not teach SEQ ID NO: 2 itself or an amino acid sequence having one or more conservative substitutions relative to SEQ ID NO: 2. Absent such a teaching, Steward cannot anticipate the invention.

Regarding claims 28 and 29

Neither can Steward anticipate the substantially pure PAMP polypeptides of claims 28 and 29, which include an amino acid sequence having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, including residues 1075 to 1382 of SEQ ID NO: 2. At best, Steward reports a sequence having 45% similarity to a subpart of SEQ ID NO: 2 but does not teach the claimed polypeptides having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, including

residues 1075 to 1382 of SEQ ID NO: 2. Thus, Steward cannot anticipate the invention of claims 28 and 29.

In view of the above, it is respectfully requested that the Examiner remove the rejection under 35 U.S.C. § 102 over Steward.

III. CONCLUSION

In view of the amendments and the remarks submitted herein, Applicant submits that the claims are in condition for allowance and respectfully requests a notice to that effect. The Examiner is invited to contact the undersigned agent or Cathryn Campbell if there are any questions relating to this application.

Respectfully submitted,

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Date

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